WELCOME TO EXPERT BRIEFINGS

Addressing the Challenge of Apathy

- The program will begin at the hour.
- Participants will be muted and off video.

Better Lives. Together.

Welcome

James Beck, PhD
Chief Scientific Officer, Parkinson's Foundation

Better Lives. Together.

Our Mission

The Parkinson's Foundation makes life better for people with Parkinson's disease by improving care and advancing research toward a cure. In everything we do, we build on the energy, experience and passion of our global Parkinson's community.

We have everything you need to live better with Parkinson's.

Poll: Getting to Know You

What best describes your connection to Parkinson's disease?

- Person with PD
- Spouse/Partner
- Parent has/had PD
- Other family
- Healthcare Professional
- Physician/Clinician
- Scientist/Researcher
- Nurse/Nurse Practitioner
- Other

For Your Convenience

Recording

Expert Briefings are recorded and archived on
www.Parkinson.org/ExpertBriefings

Better Lives. Together.

Meet Your Expert

- Bachelor's degree from the University of Michigan
- Doctorate from the Illinois Institute of Technology
- Internship at Jesse Brown VA Medical Center
- Fellowship at Rehabilitation Institute of Michigan Detroit Medical Center
- 25 years of professional experience
- Currently practicing at Northwestern Medicine-Lake Forest Hospital (2 years)
- Former psychology service manager at Shirley Ryan Ability Lab
- Experience in private practice and with NorthShore University Health System
- Extensive work with neurologic patients, including the Parkinson's disease community

Expert Briefings
Parkinson's Foundation

Addressing the Challenge of Apathy in Parkinson's

Aaron C. Malina, Ph.D., ABPP
Clinical Neuropsychologist
Northwestern Medicine-Lake Forest Hospital, A Parkinson's Foundation Center of Excellence

Better Lives. Together.

Disclosures

Parkinson's Foundation

Dr. Malina has no conflicts to disclose

Learning Objectives

Expert Briefings
Parkinson's Foundation

- Understand the clinical features of apathy in Parkinson's.
- Identify the difference between apathy and depression and when to be tested for depression.
- Learn how apathy can impact Parkinson's symptom management.
- Discuss tools to assist with the management of apathy symptoms.

A few caveats

Parkinson's Foundation

I tend to speak quickly. If I am going too fast, please make note in the chat!

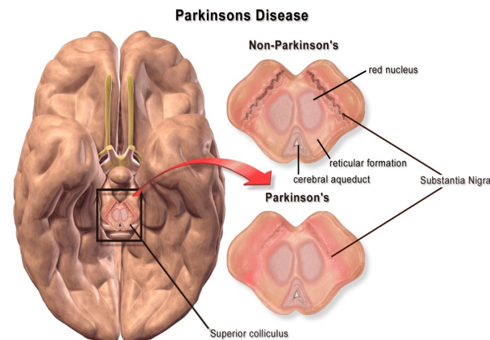
I am intentionally using some clinical terms. I want patients and families to understand clinical terms providers use. I will define everything, so it makes sense (hopefully).

There is time at the end for questions, but please feel free to post comments or questions in the chat if something is unclear or does not make sense.

Causes of Parkinson's Disease

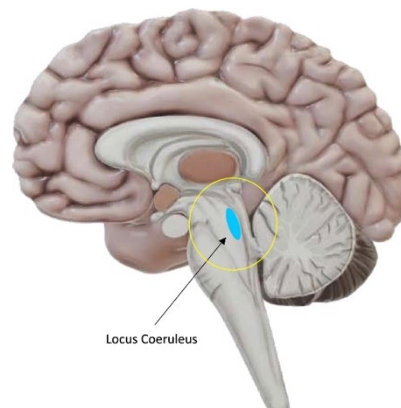
- Parkinson's disease is a degenerative disorder impacting the substantia nigra/basal ganglia AND related frontal networks
- Degeneration of the dopamine secretory cells in the substantia nigra (midbrain)-**Loss of cells that make dopamine, the chemical that plays a role in motor movement**

- Not just damage to a specific area of brain; brain's network communication very much impacted



Causes of Parkinson's Disease

- **Degeneration and disappearance of neurons in the noradrenaline system (locus coeruleus)**
  - Noradrenaline is another chemical in the brain impacting motor functioning
- **Degeneration of the:**
  - Serotonin system (emotions)
  - Acetylcholine system (thinking abilities)



Parkinson's Disease

It is more than we used to think!

Motor

- Resting tremor
- Rigidity
- Bradykinesia (slowed movement)
- Postural reflex disturbance (reflex system that keeps up upright)

Nonmotor

- Neuropsychiatric symptoms
  - Hallucinations
  - Changes in impulse control
  - Apathy
- Autonomic nervous system disorders-blood pressure, heart rate, breathing
- Cognitive changes

Parkinson's Disease: Nonmotor Symptoms

- Neuropsychiatric symptoms, including apathy are highly prevalent
- These symptoms are among the most bothersome and limiting symptoms in Parkinson's Disease
- These can be evident in the progressive and early stages of PD, starting well before motor symptoms

- Apathy is a disorder of motivation that may occur as a syndrome in itself, or as part of other neuropsychiatric disorders:
  - Depression
  - Others dementias, including:
    - Alzheimer's Disease
    - Frontotemporal Dementia
    - Lewy Body Disease.

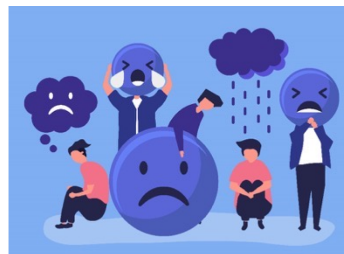
Parkinson's Foundation

DEPRESSION & ANXIETY

Parkinson's Foundation

What is depression?

- An emotional/mental health disorder
- Depression has a much broader impact than just sadness:
  - Emotions
  - Thinking
  - Perceptions of people and our environment
  - Behavior
  - Physical Health
- Depression does not require a specific event or situation to trigger it; there may be one, but it is not necessary
- 13 to 22% of PD patients



Major Depressive Disorder (MDD)

DSM-V Criteria

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful). (Note: In children and adolescents, can be irritable mood.)
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation.)
3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (Note: In children, consider failure to make expected weight gain.)
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

When to think about/screen for depression?

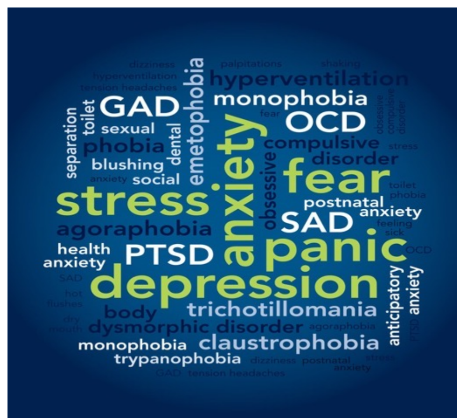
If any of the changes I just described are present, make depression a consideration

This is something we always check for as part of a regular physical examination

Anxiety in Parkinson's Disease

Parkinson's Foundation

- Can occur in up to a third of Parkinson's patients
- Higher occurrence than in the general population and many other medical conditions



Generalized Anxiety Disorder (GAD)

Parkinson's Foundation

1. The presence of excessive anxiety and worry about a variety of topics, events, or activities. Worry occurs more often than not for at least six months and is clearly excessive.
2. The worry is experienced as very challenging to control. The worry in both adults and children may easily shift from one topic to another.
3. The anxiety and worry are accompanied by at least three of the following physical or cognitive symptoms (In children, only one of these symptoms is necessary for a diagnosis of GAD):
   - Edginess or restlessness
   - Tiring easily; more fatigued than usual
   - Impaired concentration or feeling as though the mind goes blank
   - Irritability (which may or may not be observable to others)
   - Increased muscle aches or soreness
   - Difficulty sleeping (due to trouble falling asleep or staying asleep, restlessness at night, or unsatisfying sleep)

Social Phobia

Parkinson's Foundation

Marked fear or anxiety about one or more social situations in which the individual is exposed to possible scrutiny by others lasting for 6 months or more.

Fear of acting in a way that will reveal anxiety symptoms that will be negatively evaluated by others. In children, the anxiety must occur when the child is among peers and not just adults.

The social situations almost always cause fear and anxiety.

The social situations are avoided or endured with intense fear.

The fear or anxiety is out of proportion to the actual threat posed by the situation.

Anxiety in Parkinson's Disease

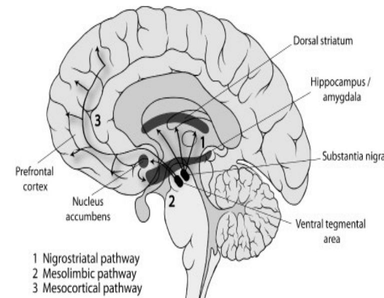
Parkinson's Foundation

- Often not recognized by medical providers
- Can have a significant negative impact on the patient and support network's quality of life
- Anxiety can impact cognitive and physical functioning
- Tends to worsen during "off" periods
- Although depression and apathy can be related in PD, this is not really the case with anxiety.

What causes mood changes in Parkinson's Disease

Parkinson's Foundation

- **Both neurobiological and psychological contributors**
- **Neurotransmitter alterations**
  - Mesial limbic dopamine pathway to amygdala (emotional center of brain)- connections between the motor and emotional areas of the brain)



Mood changes in Parkinson's Disease

Parkinson's Foundation

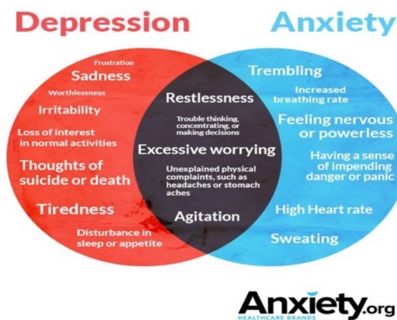
- Can have a significant negative impact on the patient and support networks' quality of life
- Mood can impact cognitive and physical functioning
- Tends to worsen during "off" periods

- Depression, unlike apathy, includes:
  - sadness
  - negative thoughts

Mood Disorders in PD

Parkinson's Foundation

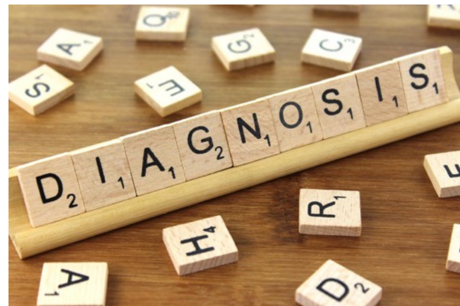
- **Greater risk for depression:**
  - Greater motor symptoms
  - Women
  - Advanced Disease
  - Cognitive Impairment
  - Genetic subtypes may have greater risk
- **Anxiety more common:**
  - Younger onset
  - Fluctuating symptoms
- All mood disorder can be associated with a lesser quality of life in PD
- Mood disorders can predate the presentation of motor symptoms



Diagnosis of Mood Disorders in PD

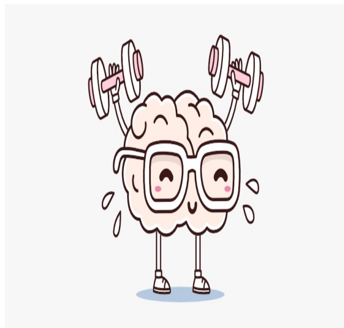
Parkinson's Foundation

- There is a low rate of self-report among patients:
  - Patients can be reluctant to acknowledge mood changes
  - Concerns more likely to come from support network
- Often confused with other physical concerns
  - Is poor sleep due to depression or PD?
- Many medical providers are primarily focused on the physical symptoms and may not ask in a detailed manner in a time limited appointment.



Treatment of Anxiety and Depression

Parkinson's Foundation



- Medication Management
- Cognitive Behavioral Psychotherapy (individual or group)
- Behavioral Activation/Exercise

Parkinson's Foundation

APATHY

What is Apathy?

Parkinson's Foundation

- **The key feature is <u>diminished motivation</u>, not attributable to:**
  - diminished level of consciousness
  - cognitive impairment (i.e thinking difficulties)
  - emotional distress
- **It is an absence of response to a stimuli as demonstrated by a lack of action**
- It is <u>not</u> just a reaction to disability; it is a neurological change
- It is both neurobiological and psychosocial

Apathy is a motivational disorder

What is Apathy?

Parkinson's Foundation

- Reduced interest in participating in main activities of life.
- Reduced effort in doing things
- Wanting to do less, not willing to start/initiate
- Trend toward withdrawal of activities
- Indifferent, disinterested or uncaring
- Little emotional expression/flat affect
- Simultaneous decrease in the behavioral, cognitive and emotional concomitants of goal directed behavior

Apathy in PD: Triad of Symptoms

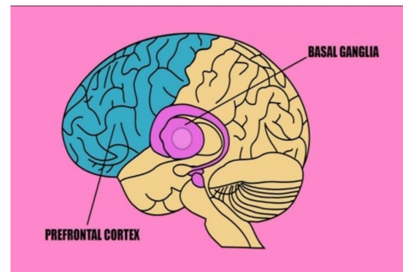
Parkinson's Foundation

- **Apathy is not unique to PD.**
  - Occurs in other neurodegenerative disorders
  - Occurs in psychiatric disorders
- **Triad/Quartet of Symptoms**
  - Behavioral
  - Cognitive
  - Emotional
  - (Social)

Behavioral Symptoms

Parkinson's Foundation

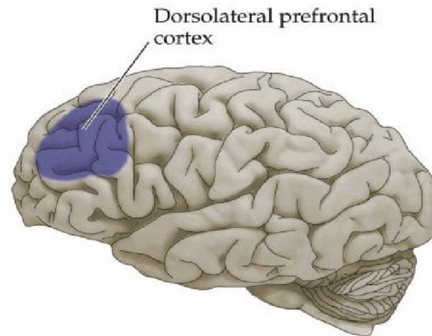
- Sometimes referred to as auto activation deficit
- Damage to the medial prefrontal cortex, basal ganglia, or globus pallidus
- Less productive
- Lacking in initiative; cognitive inertia
- Dependency on others



Cognitive Symptoms

Parkinson's Foundation

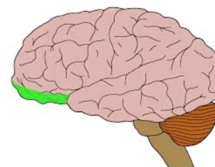
- Executive dysfunction primary
- Changes in the dorsolateral prefrontal cortex
- Decreased interest in novelty
- Lack of interest in learning new things
- Decreased ability to plan, organize and manage



Emotional Symptoms

Parkinson's Foundation

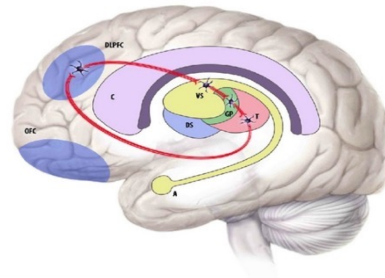
- **Emotional symptoms**
  - Sometimes referred to as the reward deficiency syndrome
  - Due to hypofunction of the orbito-medial Prefrontal Cortex
  - Blunted affect
  - Lack of responsivity to positive or negative events
  - Decreased concern about one's problems
  - Lesser self awareness
  - Emotional indifference in the face of pleasurable events and stimuli
- **Social Engagement**
  - Sometimes added to the triad
  - Engaging/actively participating in social interactions



Apathy in Parkinson's Disease

Parkinson's Foundation

- Occurs in 16 to 45% of patients
- Seen in primary PD and parkinsonism
- It is a common concern; a major neuropsychiatric feature of PD



Some studies report that PD patients suffer from apathy more often in the absence of depression than during a depressive episode.

Apathy in Parkinson's Disease

Parkinson's Foundation

- The primary issue is with incentive processing.
- Diminished capacity to process, identify, and differentiate between favorable and unfavorable outcomes to adjust subsequent behaviors accordingly.

Apathy in PD

Can contribute to:

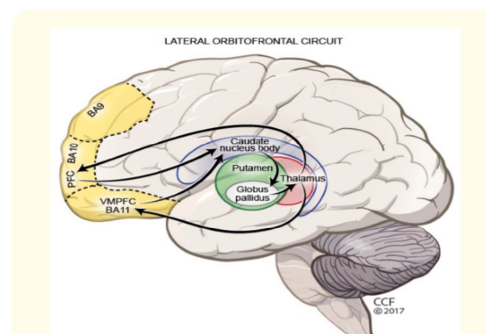
- Poor response to treatment for motor symptoms
- Greater difficulty making day to day decisions
- Increased healthcare costs

Apathy can be regarded as an independent entity caused by dysfunction of varied but related brain areas and circuits

It falls on a continuum
reduced motivated behaviors ⟶ most severe akinetic mutism (do not move or speak), abulia (absence of willpower)

Apathy in PD

- The exact pathophysiological mechanisms are unclear
- Commonly due to a dysfunction in the basal ganglia, dorsolateroprefrontal cortex, orbital frontal region, internal capsule (posterior limb), or the thalamus
- Not a specific pattern of frontal or temporal atrophy (shrinkage)



Apathy in PD

Parkinson's Foundation

- **Normally, prefrontal cortex, anterior cingulate gyrus conveys emotional information for internal/external environment to drive, plan and monitor behavior.**
- **Disruption in the frontal/subcortical circuitry**
  - Basal Ganglia Connectivity
  - Caudate Nucleus
  - Disruption in connections between prefrontal cortex and the limbic (emotional) system
  - Mesocorticolimbic pathway
- Reactive increase in D2 and D3 dopamine receptor expression or a reduction in endogenous synaptic dopamine-Less dopamine or less places to absorb it

Apathy in PD Associated with….

Parkinson's Foundation

- Increased age
- Lower premorbid educational attainment
- Depression
- Cognitive impairment
- Longer disease duration
- More frequent in patients with REM sleep behavior disorder

Apathy vs. Depression

Parkinson's Foundation

- Depression
  - Orbito-frontal/subcortical circuits may underlie depression
- Apathy
  - Mesial frontal/anterior cingulate cortex-ventral tegmental connections
- Apathy can be related to insufficient dopamine in the brain's reward circuitry (i.e., orbital prefrontal cortex—ventral striatum circuit)
- Changes in neurotransmitters pathways:
  - Cholinergic
  - Serotonergic
  - Noradrenergic
- Apathy and depression are distinct, but overlapping constructs
- Apathy can occur with or without depression or cognitive impairment

Apathy vs. Depression

Parkinson's Foundation

Apathetic symptoms

- Reduced initiative
- Decreased participation in external activities unless engaged by another person
- Loss of interest in social events or everyday activities
- Decreased interest in starting new activities
- Decreased interest in the world around him or her
- Emotional indifference
- Diminished emotional reactivity
- Less affection than usual
- Lack of concern for others' feelings or interests

Emotional symptoms of depression

- Sadness
- Feelings of guilt
- Negative thoughts and feelings
- Helplessness
- Hopelessness
- Pessimism
- Self-criticism
- Anxiety
- Suicidal ideation

Apathy vs. Depression

Parkinson's Foundation

Overlapping symptoms

- Psychomotor retardation
- Anhedonia (inability to experience joy)
- Anergia (lack of energy)
- Less physical activity than usual
- Decreased enthusiasm about usual interests

Parkinson's Foundation

COGNITION IN PARKINSON'S DISEASE

Cognitive changes in Parkinson's Disease

Parkinson's Foundation

- Cognitive decline is now recognized as a common nonmotor symptom of Parkinson's disease
- Early stages can be due to changes in dopaminergic system causing executive dysfunction. Changes in connections between the basal ganglia and thinking areas of frontal lobes
- However, other systems are also in play, with greater cognitive dysfunction:
  - Noradrenergic, Serotonergic, Cholinergic

Cognitive changes in PD

Parkinson's Foundation

- There can be progression to more global changes, but <u>not</u> all patients will progress
- Cognitive decline can be associated with:
  - Poorer quality of life
  - Increased risk of nursing home placement
  - Caregiver burden
  - Increasing health-related costs

Executive Dysfunction

Parkinson's Foundation

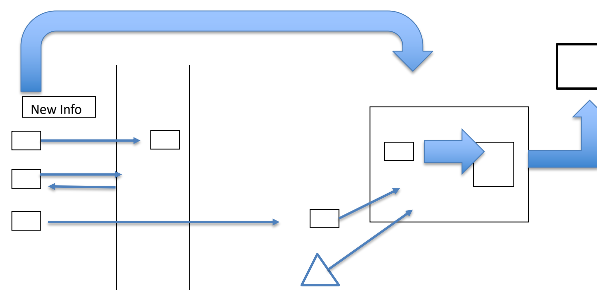
- Planning
- Organization
- Set-Shifting
- Problem solving

Apathy may be a predictor of cognitive changes in PD

How Information Gets Processed/Cognitive changes in PD

Parkinson's Foundation

Senses Attention Comprehension Memory

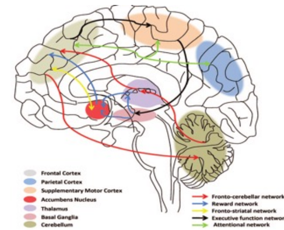


Apathy and Cognition

There is a relationship

Parkinson's Foundation

- **Greater apathy in patients with more significant cognitive impairment**
  - Several studies report an association of apathy with more severe cognitive symptoms or dementia, but apathy can also exist without cognitive dysfunction.
- **Executive dysfunction can be more common earlier on:**
  - Decreased problem solving/reasoning
  - Decreased set shifting
  - Decreased organization planning
  - Decreased working memory
- **This alters the persons capacity to associate/make sense of complex stimuli/events and emotions**



Apathy and Cognition

Parkinson's Foundation

- Apathy can be present in the early and middle stages of PD
- This can occur without the significant generalized cognitive deterioration
- However, there does tend to be related executive dysfunction

Apathy, Cognition and Depression

Parkinson's Foundation

- Both depression and apathy may derive from dysfunction of the dopaminergic mesocorticolimbic system (motor/mood network connection)
- Perhaps apathy is a specific affective system, sometimes co-occurring with depression, but involving different neural circuits.
- Depression may derive from brainstem serotonergic neuronal projections to the limbic (emotional processing) areas
- There is an association between apathy and executive dysfunction.

Impact of Apathy

Parkinson's Foundation

- Impacts quality of life with reduced participation in regular daily activities
- Introduces difficulty with clinical care and follow-up with team recommendations
- Increases caregiver burden and stress
- Reduced energy, interest, and activities may be due to apathy, but may also be part of uncomplicated PD, due to the increased effort to complete tasks/activities.

Parkinson's Foundation

ASSESSMENT

Parkinson's Foundation

Assessment

- Important to screen for depression and apathy in Parkinson's disease
- This helps to facilitate understanding and guide treatment
- The prevalence of overall apathy decreases when depression and cognitive impairment are separated out

Apathy Scales

Parkinson's Foundation

Lille Apathy Rating Scale

- Structured interview.
- 33 items, divided into nine domains.
- Responses are scored on a dichotomous scale.

Apathy Evaluation Scale

Characteristics of goal directed behavior that reflects apathy including behavioral, cognitive, and emotional indicators

- 18 items
- 18-72 (higher scores reflect more apathy)
- Items are scored on 4-point scale (not at all true, slightly true, somewhat true, very true
- Self and Informant Versions

Apathy Scales

Parkinson's Foundation

MDS-UPDRS-Apathy

- Consider level of spontaneous activity, assertiveness, motivation, and initiative and rate the impact of reduced levels on performance of daily routines and social interactions.
- The examiner should attempt to distinguish between apathy and similar symptoms that are best explained by depression.
- Instructions to patient [and caregiver]:
- Over the past week, have you felt indifferent to doing activities or being with people? [If yes, examiner asks patient or caregiver to elaborate and probes for information.]
  - 0: Normal: No apathy.
  - 1: Slight: Apathy appreciated by patient and/or caregiver, but no interference with daily activities and social interactions.
  - 2: Mild: Apathy interferes with isolated activities and social interactions.
  - 3: Moderate: Apathy interferes with most activities and social interactions.
  - 4: Severe: Passive and withdrawn, complete loss of initiative

Parkinson's Foundation

TREATMENT

Treatment for Apathy

Parkinson's Foundation

- **STN-DBS**
- **TMS**
- **Non-medication treatments**
  - Behavioral Activation
    - Therapists help to create activity plans and schedules that will lead to encounters with positively reinforcing environments

- Social engagement
- Mindfulness
- Exercise
- Increased structure
- Cognitive therapies

Treatment

- Cognitive apathy
  - Cholinesterase inhibitors
- Behavioral apathy
  - Dopamine agonists
- Emotional apathy
  - Dopamine agonists, methylphenidate, or serotonergic agents

2024 Expert Briefings

Wednesday, March 13
Understanding Pain in Parkinson's

Wednesday, April 10
Research Update: Working to Halt PD

Wednesday, May 8
Trouble with Zzz's: Sleep Challenges with Parkinson's

Wednesday, September 11
Solving the Challenge of Apathy in Parkinson's

Wednesday, October 9
More Than PD: Managing Multiple Chronic Conditions

Wednesday, November 13
What's On Your Mind? Thinking and Memory Changes in Parkinson's

Register at **Parkinson.org/ExpertBriefings**

PD Health @ Home

Weekly, virtual programs:

- Mindfulness Mondays
- Wellness Wednesdays
- Fitness Fridays
- EP Salud en Casa

Visit **Parkinson.org/PDhealth** to learn more and to register

We're Here For You

Parkinson.org

1-800-4PD-INFO
Helpline@Parkinson.org

Before You Go…

Your feedback is important to us!
Please complete the evaluation after the close of this webinar.

EXPERT BRIEFING EVALUATION

Page 1 of 1

1. What best describes your connection to Parkinson's disease (PD)?

- ☐ Person with Parkinson's
- ☐ Spouse / Partner
- ☐ Parent has / had Parkinson's
- ☐ Other family of person with Parkinson's
- ☐ Friend of person with Parkinson's
- ☐ Healthcare Professional
- ☐ Other